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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,199	05/18/2001	Masaki Hirashima	0020-4867P	5173

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,199	HIRASHIMA ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6 and 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I (claim 1-11) in Paper No. 8 is acknowledged. Accordingly, claims 1-15 are pending, claims 12-15 are withdrawn from consideration as being drawn to a non-elected invention. Therefore, claims 1-11 are examined on the merits

2. This application contains claims 12-15 drawn to an invention nonelected in Paper No. 8. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Information Disclosure Statement

3. The Information Disclosure Statement filed 8/20/01 (paper no. 6) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Drawings

4. The drawings are objected to because figure 2 is not present. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The peptide claimed reads on peptides that could be

found to exist in vivo. As such, the claimed invention has not asserted the hand of man to the invention. It is suggested that the applicant amend the claim to recite an isolated or purified peptide to obviate this rejection.

Claim Rejections - 35 USC § 112- 35 USC § 112, 2nd paragraph

6. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. With regard to claims reciting the term "fragments" or "fragment", it is unclear as to the metes and bounds of the term because the actual sequence or structure has not been adequately defined. As a result, one of skill would not know how to interpret the meaning of these terms, thereby rendering the claim indefinte.

8. With regard to claims reciting the phrase "series of peptide", it is unclear as to which peptides are included within this grouping of peptides. As such, the metes and bounds of the phrase cannot be adequately determined because it is not known what is encompassed by the term "series."

9. With regard to claims reciting the phrase "partial sequence", it is unclear as to the metes and bounds of the term because anything aside from the full length protein is considered a partial sequence, of which a deletion, truncation, or substitution of one or more amino acid could constitute a partial sequence.

10. With regard to claims reciting the phrase "wherein Xaa is selenocysteine or having a partial sequence of these amino acid sequences," it is unclear as to what is exactly meant by a partial sequence of these amino acids, because it is not clear

whether it is applicants intent to claim a partial sequence of either SEQ ID No: 1 or 2 within the Xaa amino acid.

11. With regard to claims reciting the term "protecting", it is not clear as to the extent of protection. For example, protecting from cell death could encompass eternal life of a cell, or it could imply a vaccine for which to prevent a disease state from occurring.

12. With regard to claims reciting the phrase "cells of the immune system", it is unclear as to which cells are encompassed by this phrase. There are many cells involved in the immune system, of which each has been characterized by specific phenotypes and etiologies. Therefore, because the applicant has not specifically pointed out which ones are involved in the process, the metes and bounds of the term cannot be established.

13. With regard to claims reciting the term "estimating", it is unclear as to the extent of estimation, what exactly is being assessed and what is it being compared to.

Claim Rejections - 35 USC § 112- 35 USC § 112, 1st paragraph

14. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO: 1 & 2 and therefore the written description is not commensurate in scope with the claims which read on a series of peptide fragments or variants of SEQ ID NO. 1 & 2 which, as claimed, include an peptide fragments, a series

of peptide fragments or variants wherein there are deletions, substitutions, or additions of amino acids.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO:1 & 2, the skilled artisan cannot envision the detailed structure of the encompassed series of peptide fragments or variants and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

Furthermore, although drawn specifically drawn to the DNA art the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which

defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

For example, support for peptide fragments, a series of peptide fragments or variants is provided in the specification on page 6 lines 5-25 where it is disclosed that "a series of peptide fragments as used herein refers to a group of peptide fragments with different and minute structures due to presence or absence of glycosylation, differences in electric charge, diversity in fragmentation, etc.". However, no disclosure, beyond the mere mention of peptide fragments, a series of peptide fragments or variants of te fragments is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated peptide fragment having the SEQ ID Numbers of 1 and 2 meet the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112, 1st paragraph

15. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide of SEQ ID No: 1 and 2, that is utilized as a cell death inhibitor in in vitro culture systems does not reasonably provide enablement for fragments, series of fragments or variants of selenoprotein P that is utilized as a medicament for preventing or treating disease related to cell death in an in vivo system. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or practice the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among

the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The nature of the invention: The claims of the instant invention are drawn to a peptide fragment, a series of peptide fragments wherein the series of fragments have deletions, substitutions, or additions, a medicament for protecting, preventing, and treating diseases associated with cell death, and a method of screening compounds or molecules capable of inhibiting cell-death.

The amount of direction or guidance present and the presence or absence of working examples: The specification provides examples of: the purification of selenoprotein P through various techniques ranging from heparin columns to HPLC, the analysis of the protein extracted from the columns, the production of anti-selenoprotein P antibodies, the purification of selenoprotein P protein and fragments (SEQ ID No: 2, 4, and/or 5) having molecular weights of 10-30 kDa, and the activity of the fragments purified. However, no where in the specification does it teach specifically any other fragments or series of fragment that have cell-death inhibitory activity. Furthermore, the specification does not teach how these protein fragments are to be used as a medicament for the protection, prevention, or treatment of disease associated with cell death.

One of skill in the art would be forced to experiment to determine these other fragments because the specification has only taught a general description of the other fragments or series of fragments, wherein the fragments are isolated from plasma

proteins and have molecular weights of 10-30 kDa. There are many proteins or possibly degradation products that are founding the plasma of blood that fulfill the general physical description taught by the specification. ***Because the activity of the fragments or series of fragments is an intended use, it does not breath any meaning into the interpretation of the claims.*** As such one of skill in the art would need to fractionate and screen all the numerous proteins or protein fragment found in the plasma. Furthermore, a medicament implies the in vivo usage of a product, of which there has been no detail disclosure presented. A medicament intended for administration to a subject has to be produced as to not have deleterious effects on a subject, be active upon administration to a subject, be stable prior to administration, and formulated with specific compounds or molecules. Because one of skill in the art does not even know the structure and amino acid make-up of the series of peptides or for that matter the peptide fragments in general, the skilled artisan would be forced to experiment with medicaments of which there is no known composition, thereby administrating and testing for side effects and not knowing what to expect. And lastly, one of skill in the art has not been provided enough teaching or disclosure to ensure that the medicament would even work in vivo. Because there is a lack of this knowledge, how can one expect that treatment, prevention, or protection is even feasible. Surely, protection or prevention is not possible because one of skill in the art would not even know who would be at risk of developing a cell-death related disease. For example, how would one know to administer the medicament to prevent or protect against AIDS before the contration of the virus? Furthermore, to protect against cell

death implies an eternal protection of cells from dying and thereby a medicament for eternal life.

The breadth of the claims and the quantity of experimentation needed: Given the broad range of peptide fragment encompassed by the criteria of isolation, the unknown consequences and formulation of the medicament, and the lack of teaching describing the trerating, prevention, or protection of diseases associated with cell-death, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1,5,6, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Rafferty *et al* (Biochem J 1998 May 15;332(Pt1):231-6). It is noted that foreign priority is claimed to a Japanese document (JP 347863/1998) filed 11/19/1998, however, the document is in Japanese and a determination of proper priority cannot be made. If the applicant is able to provide the proper documentation as to receive priority to the Japanese document, the instant rejection can be made under 35 USC 102(a).

The claims of the instant invention is drawn to a peptide fragment or a series of peptide fragments which have cell death inhibitory properties, is characterized by bands of 3-4, 7-9, and 10-12 kDa on a SDS-page gel under reducing conditions, is a medicament for treating, preventing or protecting from disease associated with cell death, and is an additive for cell culture.

Rafferty *et al* teach the isolation of peptide fragments that have cell death inhibitory properties, range in size from approximately 10-60 kDa as determined by SDS-Page gel electrophoresis under reducing conditions, capable of treating a disease associated with cell death, and is added in cell cultures. In the absence of evidence to the contrary, because it is well known in the art that size determination by SDS-Page electrophoresis is an approximate estimation and because sizes as small as 3-9 kDa are often difficult to distinguish from 10 kDa, it is anticipated.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
December 4, 2002